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TITLE: Integrin-binding peptides

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INVENTOR-INFORMATION:

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CLAIMS:

We claim:

1. A peptide that binds to .alpha..sub.v .beta..sub.3 integrin and that contains the sequence RLD in a constrained secondary conformation.
2. The peptide of claim 1, wherein the sequence RLD is contained in a nine-membered cycle.
3. The peptide of claim 3, wherein the cycle is formed from a disulfide bond, a peptide bond or a lactam bond.
4. The peptide of claim 3, wherein the sequence RLD is further contained in the sequence CX.sub.1 X.sub.2 RLDX.sub.3 X.sub.4 C (SEQ ID NO: 38), wherein X.sub.1, X.sub.2, X.sub.3 and X.sub.4 are any amino acid; CARRLDAPC (SEQ ID NO: 19) or CPSRLDSPC (SEQ ID NO: 20).
5. A peptide that binds to an integrin and that contains the sequence X.sub.1 X.sub.2 X.sub.3 RGDX.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3), wherein X.sub.1, X.sub.3, X.sub.4 and X.sub.6 are involved in the formation of two bridges and X.sub.2 and X.sub.5 are 1 to 5 amino acids.
6. The peptide of claim 5, wherein said peptide binds to .alpha..sub.v .beta..sub.3 and .alpha..sub.v .beta..sub.5 integrins.
7. The peptide of claim 5, wherein said two bridges formed by X.sub.1, X.sub.3, X.sub.4 and X.sub.6 are disulfide bonds, peptide bonds or lactam bonds.
8. The peptide of claim 7, wherein the sequence X.sub.1 X.sub.2 X.sub.3 RGDX.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3) is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15), CDCRGDCFC (SEQ ID NO: 16), CDCRGDCLC (SEQ ID NO: 17), or CLCRGDCIC (SEQ ID NO: 18).
9. A method useful for attaching cells to a substrate, comprising binding a

- peptide of claim 5 to a substrate and contacting the substrate with the cell.
10. The method of claim 9, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
11. A patch graft, comprising a peptide of claim 5 attached to a support matrix.
12. The patch graft of claim 11, wherein the support matrix comprises collagen, glycosaminoglycan or proteoglycan.
13. The patch graft of claim 11, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
14. The patch graft of claim 13, wherein the support matrix comprises collagen, glycosaminoglycan or proteoglycan.
15. A method useful for promoting wound healing, comprising applying to the wound a patch graft of claim 11.
16. A method useful for promoting wound healing, comprising applying to the wound a patch graft of claim 13.
17. A method useful for inhibiting the attachment of osteoclasts to bone, comprising administering to an individual a peptide of claim 5.
18. The method of claim 17, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
19. A method useful for inhibiting angiogenesis, comprising administering to an individual a peptide of claim 5.
20. The method of claim 19, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
21. A method useful for inhibiting metastasis of a tumor expressing .alpha..sub.v .beta..sub.3 integrin, comprising administering to an individual a peptide of claim 5.
22. The method of claim 21, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
23. A method useful for inhibiting migration of smooth muscle cells, comprising administering to an individual a peptide of claim 5.
24. The method of claim 23, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).
25. A pharmaceutical composition, comprising a peptide that binds to .alpha..sub.v .beta..sub.3 integrin and that contains the sequence RLD in a constrained secondary conformation, and a pharmaceutically-acceptable carrier therefor.
26. A pharmaceutical composition, comprising a peptide that binds to an integrin and that contains the sequence X.sub.1 X.sub.2 X.sub.3 RGD X.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3), wherein X.sub.1, X.sub.3, X.sub.4 and X.sub.6 are involved in the formation of two bridges and X.sub.2 and X.sub.5 are 1 to 5 amino acids.
27. A pharmaceutical composition, comprising a peptide of claim 26 that binds to .alpha..sub.v .beta..sub.3 and .alpha..sub.v .beta..sub.5 integrins, and a pharmaceutically-acceptable carrier therefor.

28. The pharmaceutical composition of claim 26, wherein said peptide is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).

29. A peptide that selectively binds .alpha..sub.5 .beta..sub.1 integrin and that contains the sequence RGDGX (SEQ ID NO: 2), wherein X is a tryptophan residue, wherein the sequence RGDGX (SEQ ID NO: 2) is contained in a seven-membered or nine-membered cycle, wherein the cycle is formed by a disulfide bond, a peptide bond or a lactam bond, and wherein the sequence RGDGX (SEQ ID NO: 2) is further contained in the sequence CRGDGXC (SEQ ID NO: 30).

30. The peptide of claim 8, wherein the sequence X.sub.1 X.sub.2 X.sub.3 RGDY.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3) is CX.sub.2 CRGDCX.sub.5 C (SEQ ID NO: 15).

31. The peptide of claim 8, wherein the sequence X.sub.1 X.sub.2 X.sub.3 RGDY.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3) is CDCRGDCFC (SEQ ID NO: 16).

32. The peptide of claim 8, wherein the sequence X.sub.1 X.sub.2 X.sub.3 RGDY.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3) is CDCRGDCLC (SEQ ID NO: 17).

33. The peptide of claim 8, wherein the sequence X.sub.1 X.sub.2 X.sub.3 RGDY.sub.4 X.sub.5 X.sub.6 (SEQ ID NO: 3) is CLCRGDCIC (SEQ ID NO: 18).

34. The pharmaceutical composition of claim 26, wherein said peptide is CDCRGDCFC (SEQ ID NO: 16).

35. The pharmaceutical composition of claim 26, wherein said peptide is CDCRGDCLC (SEQ ID NO: 17).

36. The pharmaceutical composition of claim 26, wherein said peptide is CLCRGDCIC (SEQ ID NO: 18).